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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,576	12/05/2003	Praveen Sharma	Q65721	8084
23373 7590 06/12/2009 SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037				
EXAMINER				
SWITZER, JULIET CAROLINE				
ART UNIT		PAPER NUMBER		
1634				
MAIL DATE		DELIVERY MODE		
06/12/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/727,576

**Applicant(s)**

SHARMA ET AL.

**Examiner**

Juliet C. Switzer

**Art Unit**

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 March 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 18-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SG/US)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. This office action is written supplemental to the FINAL office action mailed 8/18/08. This action differs from the previous action because it includes 112 2nd paragraph rejections that were not included in the previous final office action. **This action is FINAL.**
2. It is noted that "very early stage breast cancer" is understood to refer to stage 0 breast cancer which includes ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) (see declaration filed 9/21/07, pages 1 and 2). Thus, the recitation in the claims of "very early stage breast cancer" is interpreted as referring to these two types of cancer.

#### ***Claim Rejections - 35 USC § 103***

3. Claims 18 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ralph et al. (US 6,190,857; as cited in IDS) in view of Lukas et al. (Journal of Investigative Medicine, 1997, Vol. 45, No. 1, page 132A).

The rejection is maintained as set forth in the office action mailed 8/18/08.

4. Claims 19, 26, 27, 28, 29, 30, 31, 32, 33, 34, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ralph et al. in view of Lukas et al. as applied to claims above, and further in view of Wadhwa et al. (Molecular Biotechnology, Volume 6, pages 213-217).

The rejection is maintained as set forth in the office action mailed 8/18/08.

#### ***Double Patenting***

5. The double patenting rejection over claims 1-36 of copending Application No. 11/149370 is WITHDRAWN in view of the amendment of those claims to be limited to methods where the disease is multiple sclerosis.

### **Response to Remarks**

Applicant continues to traverse the rejections under 103 and relies upon a declaration filed by Dr. James Mackay. The declaration has been fully considered but is not persuasive to overcome the rejection.

Dr. Mackay states that he believes that the skilled person reading Ralph et al. would have understood that the method described by Ralph et al. was based on the release of cancer cells, their debris, or cellular components into the blood system resulting in direct interaction between cancer cells and the blood cells, thereby affecting gene expression of the blood cells (paragraph 5). However, this is in direct contrast to the express teachings of Ralph et al. which teaches "...since the markers are produced by circulating leukocytes rather than diseased cells, it is expected that detection may be feasible at very early stages of disease progression, when there are few or no circulating cells present in the peripheral blood (Col. 5, lines 7-11)."

Dr. Mackay points to two passages from Ralph et al. to support an assertion that Ralph et al state that direct contact between the sample to be analyzed and the diseased cells is necessary. Both of these passages are in a portion of Ralph et al. that discusses Immunodetection Assays, not the identification of markers based on mRNA expression. When Ralph et al. discuss the identification of markers based on differential mRNA expression, their only qualification for the sample is that it be a tissue or fluid where leukocytes may be present (Col. 53, lines 1-5). There is no mention that it is required or even preferred that there be direct interaction between cancer cells or their debris or cellular components.

The declaration states that "the skilled person would believe that the Ralph et al. method could only be extended to cancers in which contact between the cancer cells and peripheral blood cells occurred (paragraph 9)." The declaration suggests that this happens only once cells with metastatic potential or metastasis appear. However, this opinion is contraindicated by the express teachings of Ralph et al. and the general knowledge of the constantly circulating function of white blood cells. At the time the invention was made, one of ordinary skill in the art certainly would have known that white blood cells spend most of their time outside the circulatory system, patrolling through interstitial fluid and the lymphatic system (Campbell, 1996, page 833). So, it would have been expected that leukocytes would have come in contact with the tumor cells, even if no blood vessels had invaded the tumor. This is reflected in Ralph et al.'s express teaching that detection would be feasible even when there are few of no circulating cancer cells, as stated by Ralph et al., at very early stages of disease progression.

### ***Conclusion***

6. No claim is allowed.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Tuesday or Wednesday, from 9:00 AM until 4:30 PM, and Thursday afternoon from 12:30 PM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached by calling (571) 272-0763.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this

application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Juliet C. Switzer/  
Primary Examiner  
Art Unit 1634

June 12, 2009